AMENDMENTS TO THE DRAWINGS

Please replace the original drawing sheet containing Figure 4C with the attachment replacement sheet of corrected drawing Figure 4C.

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1 and 2 were pending in this application when last examined and stand rejected.

Claim 1 was also objected to.

Claims 1 and 2 are amended, and claim 3 is newly added.

Support for the amendment to claim 1 can be found in the disclosure, for example, at page 3, lines 6-11, page 5, line 28 to page 6, line 2, and original claim 1.

Support for the amendment to claim 2 can be found in the disclosure, for example, at page 3, lines 6-11, and original claim 2.

Support for new claim 3 can be found in the disclosure, for example, at page 4, lines 11-12, 19-20, page 8, lines 18-24. Support can also be found in the working examples. See for instance, examples 2.2-2.4 on pages 15-18.

No new matter has been added

Claims 1-3 are pending upon entry of this amendment.

The Specification and Abstract have been revised to correct the grammatical and typographical errors noted in the Office Action.

The Specification in the Brief Description of the Drawings on page 4 has been amended to provide the appropriate SEQ ID NOS for the sequences depicted in Figs. 1 and 2 as suggested by the Examiner. The Specification is also amended to replace the Sequence Listing of record with the attached substitute Sequence Listing. Support for these amendments can be found in the originally filed specification at the same locations and in the newly revised Sequence Listing. No new matter has been added.

Enclosed herewith is a revised substitute Sequence Listing in both paper and computer readable form (CRF) which replaces the Sequence Listing of record. Amendments directing its entry into the specification have been incorporated herein. The content of the paper and computer readable copies are the same and no new matter has been added. The CRF has been run through Checker and no errors were found.

Therefore, the application is in compliance with the sequence rules under 37 C.F.R. § 1.821-1.825.

A replacement drawing sheet for Figure 4C is enclosed, which corrects the spelling error noted by the Office. No new matter has been added.

II. OBJECTION TO THE SPECIFICATION

The Specification was objected for containing the minor informalities noted in item 2 on page 2 of the Office Action.

The attached revised substitute Specification corrects the noted minor informalities, thereby overcoming this objection.

III. OBJECTIONS TO THE DRAWINGS

The drawings were objected to for the informalities noted in items 3 and 4 on page 2 of the Office Action.

The present amendment overcomes these objections. In particular, the Brief Description of the Specification has been amended to include SEQ ID NOs for the sequence recited in Figures 1 and 2.

Also, enclosed herewith is a replacement drawing sheet for Figure 4C. The term "titre" in original Figure 4C has been replaced with "titer" as suggested by the Office.

Thus, the drawing objections are untenable and should be withdrawn.

IV. CLAIM OBJECTION

In item 5 on page 3 of the Action, claim 5 was objected to for reciting "which a third" in line 3.

The present amendment overcomes this objection by amending claim 1 to recite "which the third" as suggested by the Office, thereby correcting this grammatical error.

V. INDEFINITENESS REJECTIONS

Claims 1 and 2 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons set forth in items 7 and 8 on page 4 of the Action.

Applicants respectfully submit that the present amendment overcomes the rejections.

To start, the claims have been amended to define what is intended by the phrase "without a change" in claim 1. In particular, the amended claims specify that DNA substitution does not change the amino acid sequence encoded by the codon. Support can be found in the disclosure, for example, at page 3, lines 6-11, page 5, line 28 to page 6, line 2.

Claim 2 is amended to remove the objected language "total positions" and add the phrase "the first and second positions of each codon". The added limitation clearly defines the substitution positions.

Claim 2 is further amended to remove the objected language "type of amino acid" and"as much as possible".

It is respectfully submitted that the skilled artisan, upon reading this disclosure and in view of the knowledge in the art, would clearly understand this language to mean that the codons in the DNA sequence can be altered without changing the amino acid sequence encoded thereby.

For these reasons, it is respectfully submitted that the above-noted indefiniteness rejections are untenable and should be withdrawn.

VI. ANTICIPATION REJECTION

In item 10 on page 5 of the Action, claims 1 and 2 were rejected under 35 U.S.C. § 102(b) as anticipated by Bloom et al. (US 5,504,005) in light of Andersson et al. (Microbiology, Vol. 142, pp. 915-925, 1996).

Applicants respectfully traverse this rejection as applied to the amended and new claims.

Bloom et al. discloses a recombinant BCG vaccine transformed with polynucleotides from *M. tuberculosis*. Andersson et al. was relied upon as evidence that genes from *M. tuberculosis* inherently comprise a high G - C richness at the third position of each codon.

On the other hand, the amended claims require the polynucleotide for insertion to be artificially modified so that the third position of each codon is substituted with G or C without changing the amino acid sequence encoded thereby. Bloom et al. and Andersson et al. fail to disclose or suggest such artificial modifications.

In addition, Applicants respectfully submit that the effects of the present invention clearly differ from those for the recombinant BCG vaccine of the cited prior art. The effect of the recombinant vaccine of Bloom et al. is provide long-term stimulation of immunity. On the other hand, the effect of the present invention is to induce a sufficient immune response at low doses. See, the description at page 2, lines 23-28, and examples 2.2-2.4 on pages 15-18. This is important, because, as disclosed in the specification at page 2, lines 1-7:

> the conventional recombinant BCG vaccine has not always been sufficient in its capability of inducing immunity to infection, cancer, or the like to be provided as a target. For example, in the case of immunizing a guinea pig with a recombinant BCG vaccine targeted at HIV-1, it should be dosed 10 to 100 times higher than a typical dosage (0.05 to 0.1 mg) of BCG vaccine generally used for human.

Bloom et al. and Andersson et al. simply do not disclose or suggest artificial modifications of codon usage for inducing a sufficient immune response at low doses. Therefore, Applicants respectfully submit that the amended claims are novel over Bloom et al. and Andersson et al.

Lastly, it is respectfully submitted that Bloom et al. do not disclose or suggest the subject matter of new claim 3. This claim is drawn to a recombinant BCG vaccine capable of expressing

HIV-1 antigenic protein. See examples 2.2-2.4 on pages 15-18. Accordingly, this new claim is also novel over Bloom et al. and Andersson et al.

For these reasons, the above-noted 102(b) anticipation rejection over Bloom et al. and Andersson et al. is untenable and should be withdrawn.

VII. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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By: _____

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September 28, 2007

ATTACHMENTS

1. Clean version of revised Abstract;

2. Substitute Specification (marked-up copy);

3. Substitute Specification (clean copy);

4. Revised Sequence Listing (paper & CRF);

5. Replacement drawing sheet for Figure 4C.